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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,463	10/14/2004	Yuval Simha Landschaft	RO0908US (#905668)	9282

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EXAMINER	
MOHAMED, ABDEL A	

ART UNIT	PAPER NUMBER
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,463	LANDSCHAFT, YUVAL SIMHA	
	Examiner	Art Unit	
	Abdel A. Mohamed	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 8-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 8-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

ACKNOWLEDGMENT TO AMENDMENT, REMARKS AND STATUS OF THE CLAIMS

1. The amendment and remarks filed 04/23/07 are acknowledged, entered and considered. In view of Applicant's request claims 1, 5, 8, 9, 12, 14 and 16 have been amended and claim 7 has been canceled. Claims 1-6 and 8-16 are now pending in the application. The objection to the claims and the rejections under 35 U.S.C. 102(a) and (e) are withdrawn in view of Applicant's amendment and remarks filed 04/23/07. However, the rejection under 35 U.S.C. 103(a) over the prior art of record is maintained for the same reasons set forth in the previous Office action.

OBJECTION TO THE CLAIMS

2. Claims 14 and 15 are objected because the claims as drafted are directed to use claims, which is not standard U.S. practice. Amending the claims to method claims would obviate this objection. Appropriate correction is required.

ARGUMENTS ARE NOT PERSUASIVE

CLAIMS REJECTION-35 U.S.C. § 103(a)

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6 and 8-16 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Kirby et al (U.S. Patent No. 6,444,234) taken with Yamamoto et al (U.S. patent No. 5,759,445), Guo et al (Drug Deliv. Vol. 7, No. 2, pp. 113-116, 2000) and Thorand et al (Southeast Asian J. Trop. Med. Public Health, Vol. 24, No. 4, pp. 624-630, 1993).

Applicant's arguments filed 04/23/07 have been fully considered but they are not persuasive. Applicant has argued that to establish a p*rima facie* case of obviousness, three basic criteria must be met, as set forth in M.P.E.P. § 2142. First, there must be some suggestion or motivation to modify the reference or to combine the reference teachings. Second, there must be reasonable expectation of success. Third, the prior art reference (or references when combined) must teach or suggest all the claim limitations. Applicant continues by stating that by way of a brief summary of the present invention, it is provided that therapeutically active polypeptides or ionic nutrients can be administered through the human skin if a non-oily emulsion of lecithin, bile salts and cholesterol in water is utilized. Despite considerable effort, such an invention simply has not yet been achieved. In particular, the prior art has not yet achieved providing a reliable system for transdermal administration of polypeptides or ions, which would enable transdermal administration of insulin to a diabetic patient at a therapeutically sufficient rate and without providing a risk of hypoglycemia. Further, Applicant states that the primary reference of Kirby et al ('234 patent) teaches a composition for rapid and non-irritating transdermal delivery of pharmaceutically active agents and provides a formulation, which includes:

(A) at least one solvent in which the active agent is soluble;

(B) at least one solvent modifier having a common structural features as that of the active agent and comprising an ethylenically unsaturated polar group;

(C) at least one metabolizable solute modifier;

(D) at least one source of cellular activation energy; and

(E) at least one skin stabilizer .

Thus, the crucial aspect of the formulation of '234 patent is the presence of Forskolin or other source of cellular energy (D), namely, induction of cAMP or cGMP, and the source of cellular activation energy is an essential component of the liquid carrier composition for the transdermal delivery of medicament, as taught by the primary reference of Kirby et al. To the contrary , the composition for transdermal administration of a therapeutically active compound or nutrient according to the present invention **does not contain a source of cellular activation energy** (emphasis added). Moreover, one skilled in the art cannot and would not infer from '234 patent disclosure that a source of cellular activation energy may be omitted from the liquid carrier composition without impairing the desired transdermal delivery of a medicament. Thus, the primary reference of Kirby et al does not make a formulation obvious which does not contain a source of cellular activation energy.

In addition, the secondary reference of Guo et al teach the utility of specifically designed flexible vesicles for transdermal delivery of insulin, wherein these specific vesicles comprise sodium cholate. However, the composition of the present invention does not contain sodium cholate, but rather cholesterol. Although cholesterol and

sodium cholate are structurally similar molecules, Guo et al does not provide any motivation or teaching (or any other information) that replacing sodium cholate with cholesterol would also yield flexible vesicles displaying improved transdermal delivery of insulin. Further, Applicant argues that the secondary reference of Yamamoto et al teach an aqueous lipid-dispersed solution having a dispersion form and particle size which are similar to those of serum lipids. The lipid-dispersed solution is obtained by evaporating an organic solvent from a mixture prepared by adding cholesterol, a phospholipids, bile acid salts and a neutral lipid and/or cholesterol ester to the organic solvent. Applicant notes that the aqueous dispersed solution according to Yamamoto et al **is not intended** (emphasis added) for transdermal drug delivery. The aqueous dispersed solution is merely a standard solution for determining lipid levels in sera. Yamamoto et al does not indicate or teach at all that the standard solution may be employed for transdermal drug delivery. Furthermore, the secondary reference of Thorand et al pertains to the bioavailability of iron but does not relate to transdermal administration of iron. Thorand et al solely disclose iron tablets and therefore pertain to an oral administration of iron. Therefore, Thorand et al does not provide any information or teaching toward the transdermal administration of iron. In turn, the present invention cannot have been made obvious even if the combination of references include the teachings of Thorand et al. Applicant concludes by stating that the present invention defined in the presently amended claims is patentably distinguishable over the combination of prior art teachings under 35 U.S.C. 103(a) because one skilled in the art would not be motivated to combine said references to

modify the primary reference's of Kirby et al to arrive at the presently claimed invention. Thus, the primary reference either singularly or in combination with the secondary references fails to teach or make obvious the utility of a non-oily emulsion, which is a mixture of lecithin, bile salts and cholesterol in water intended for transdermal administration, is not persuasive.

Contrary to Applicant's arguments, as stated in the previous Office action, the primary reference of Kirby et al ('234 patent) as discussed above discloses a composition for transdermal administration of at least one therapeutically active compound (polypeptide) or nutrient (Vitamins), said composition comprising one item selected from the group consisting of at least one therapeutically active compound such as antibiotics drugs and at least on nutrient and a non-oily emulsion (cholesterol), wherein the polypeptide has a molecular weight of 500 D and higher (overlaps with the range of up to 7000 kDa of claim 5) and further comprising an organic sulfur compound (methylsulfonylmethane), wherein the composition for transdermal administration of active substance which is nutrients and/or medications are useful as a cream, gel, lotion, ointment and patch (See, e.g. cols 1, 5-11, 15, 31 and 32) as directed to claims 1, 2, 4-6, 11 and 13-15.

With respect to Applicant's arguments that the present invention does not contain a source of cellular activation, which is taught by the primary reference's of Kirby et al, is unpersuasive. Contrary to Applicant's arguments, independent claim 1 is open-ended, in view of the "comprising" and allows for additional ingredient, component or step, and as such, there is no clear indication in the specification or claims to determine

the ingredient, component or step included versus excluded, the claims must be read in light of the specification. Since Applicant has failed to establish the exclusion of "formulation containing a source of cellular activation energy", and not defined in the instant specification, independent claim 1 as drafted is read as "comprising" (i.e., open-ended), and as such Applicant's arguments that the primary reference of Kirby et al is drawn to the use of a formulation containing a source of cellular activation energy *per se* is unpersuasive. Further, the limitations Applicant argued with (i.e., exclusion of a formulation containing a source of cellular activation energy) are not recited in the rejected claims. Nevertheless, the claims are interpreted in light of the specification; limitations from the specification are not read into claims. See *In re Geuns*, 988 F.2nd 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Thus, Applicant's argument is not commensurate to the scope of the claims.

In regard to Applicant's arguments that the secondary reference's of Yamamoto et al teaching is not intended for transdermal drug delivery, rather, the aqueous dispersed solution is merely a standard solution for determining lipid levels in sera. Thus, Yamamoto et al does not indicate or teach at all that the standard solution may be employed for transdermal drug delivery is not persuasive. Although, the secondary references of Yamamoto et al or Thorand et al do not disclose the use of transdermal drug delivery, however, the primary reference of Kirby et al discloses such use of transdermal drug delivery; nevertheless, a statement of usefulness or contemplated use of a claimed compound or composition in a claim is usually given little weight in distinguishing over the prior art. *In re Maeder et al.* (CCPA 1964) 337 F2d 875, 143

USPQ 248; *In re Riden et al.* (CCPA 1963) 318 F2d 761, 138 USPQ 112; *In re Sinex* (CCPA 1962) 309 F2d 488, 135 USPQ 302. Further, it is well established that the intended use of a compound (e.g., a polypeptide or a protein or a glycoprotein) does not impart patentability to the compound. *In re Spada,* 911 F.2d 705, 15 USPQ2d 1655 (Fed. Cir. 1990) (The discovery of a new property or use of a previously known composition, even when that property and use are unobvious from the prior art, can not impart patentability to claims to the known composition); *In re Pearson*, 494 F.2d 1399, 1403, 181 USPQ 641, 644 (CCPA 1974) (intended use of an old composition does not render composition claims patentable); *In re Zierden*, 411 F.2d 1325, 1328, 162 USPQ 102, 104 (CCPA 1969).

The Examiner acknowledges and reiterate the previous Office action that the primary reference of '234 patent differs from claims 1-6 and 8-16 in not teaching the use of non-oily emulsion which is a mixture of lecithin, bile salt and cholesterol with the specific ratio and amount disclosed in the claims, and the use of a nutrient which is an ionic compound and the ionic compound is a metal ion. However, the secondary reference of Guo et al discloses a study of transdermal delivery of insulin (therapeutically active compound and/or peptide) in mice by using lecithin vesicles as a carrier. The study was undertaken to characterize the preparation of flexible lecithin vesicles containing insulin and to assess the enhancing effect of these flexible vesicles on the transdermal delivery of a hydrophilic proteins or polypeptides. The reference concludes by stating flexible vesicles may become a promising carrier for transdermal delivery of hydrophilic polypeptides (See e.g. Abstract and Discussion). Further, the

secondary reference of Yamamoto et al ('445 patent) discloses an aqueous dispersed solution, which comprises the steps of evaporating an organic solvent from a mixture prepared by adding cholesterol, lecithin, a surfactant and a neutral lipid, and/or a cholesterol ester in the organic solvent in a specific range of the concentration ratio. The preferred weight ratio of the sum of the cholesterol and cholesterol ester to the lecithin is from 1:1 to 1:2, a weight ratio of the neutral lipid to the lecithin is from 1:10 to 1:5, and a concentration of the lecithin is not more than 1,000 mg/dl when the lecithin is finally dispersed in a water or buffer (See e.g. Summary of the Invention and claim 4) as directed to claims 1 and 8-10. Thus, utilizing the mixtures of non-oily emulsion of lecithin, bile salt and cholesterol is a choice procedure as pointed out by the secondary reference of '445 patent, and as such use of non-oily emulsion which is a mixture of lecithin, bile salt and cholesterol is deemed to be obvious to one of ordinary skill in the art because the skilled artisan would reasonably have expected that use of non-oily emulsion such as lecithin would have resulted as a promising carrier for transdermal delivery of hydrophilic polypeptides as taught by the secondary reference of Guo et al. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to employ a composition for transdermal administration of the primary reference because such features are known or suggested in the art, as seen in the secondary reference, and including such features (i.e., use of non-oily emulsion which is a mixture of lecithin, bile salt and cholesterol in water) into a composition for transdermal administration of at least one therapeutically active compound (polypeptide) or nutrient (Vitamins), said composition comprising one item selected from the group

consisting of at least one therapeutically active compound such as antibiotics drugs and at least on nutrient and a non-oily emulsion (cholesterol), wherein the polypeptide has a molecular weight of 500 D and higher and further comprising an organic sulfur compound (methylsulfonylmethane), wherein the composition for transdermal administration of active substance which is nutrients and/or medications are useful as a cream, gel, lotion, ointment and patch.

With respect to the limitations of a nutrient, which is an ionic compound and the ionic compound, is a metal ion, the secondary reference of Thorand et al demonstrates that the administration of iron (metal ion) supplement is an effective intervention in treating anemia caused by iron deficiency. Thus, the reference shows the administration of at least one therapeutically active compound and said at least one nutrient is an ionic compound and wherein the ionic compound is a metal ion (i.e., iron as a nutrient), and as such meet the limitation of claim 2 and 3.

Thus, in view of the above, it would have been *prima facie* obvious to one of ordinary skill in the art to combine the primary reference's teaching of a composition for transdermal administration into secondary references teachings because the secondary reference teach the use of non-oily emulsion which is a mixture of lecithin, bile salt and cholesterol, and the use of a nutrient which is an ionic compound and the ionic compound is a metal ion. Because use of non-oily emulsions and a nutrient ionic compound which is a metal ion are known and suggested in the art as seen the secondary references, and including such features into the composition of the primary reference which teaches a composition for transdermal administration of at least one

therapeutically active compound (polypeptide) or nutrient (Vitamins), said composition comprising one item selected from the group consisting of at least one therapeutically active compound such as antibiotics drugs and at least on nutrient and a non-oily emulsion (cholesterol), wherein the polypeptide has a molecular weight of 500 D and higher and further comprising an organic sulfur compound (methylsulfonylmethane), wherein the composition for transdermal administration of active substance which is nutrients and/or medications are useful as a cream, gel, lotion, ointment and patch would have been obvious to one of ordinary skill in the art to obtain the known and recognized functions and advantages thereof.

Therefore, in view of the above and in view of the combined teachings of the prior art; one of ordinary skill in the art would have been motivated at the time the invention was made to use the already known composition for transdermal administration comprising therapeutically active compound such as polypeptides and antibiotic drugs, nutrients such as vitamins, ionic compounds which are metal ions and non-oily emulsions such as lecithin, bile salt and cholesterol and further comprising organic sulfur compounds such as methylsulfonylmethane (MSM), wherein the composition for transdermal administration of active substance which is nutrients and/or medications are useful as a cream, gel, lotion, ointment and patch, absent of sufficient factual evidence or unexpected results to the contrary.

Although, the prior art does not teach the specific amounts of lecithin, bile salts, cholesterol and organic sulfur, and the ratio of by weight of lecithin, bile salts and cholesterol as claimed, however, the ranges claimed and cited by the prior art overlaps,

and as such the selection of the appropriate specific amounts of lecithin, bile salts, cholesterol and organic sulfur, and the ratio of by weight of lecithin, bile salts and cholesterol is conventional and within the ordinary skill of the art to which this invention pertains. Therefore, the claimed specific amounts of lecithin, bile salt, cholesterol and organic sulfur, and the ratio of by weight of lecithin, bile salts and cholesterol, which fall within the scope of the prior art would have been *prima facie* obvious from said prior art disclosure to a person of ordinary skill in the art at the time the invention was made because in the absence of sufficient objective factual evidence or unexpected results to the contrary, Applicant's claims are directed to optimization of an "art recognized variable" which is well within the purview of one of ordinary skill in the art, *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980). Thus, it is made obvious by the teachings of the prior art since the instantly claimed invention which falls within the scope of the prior art teachings would have been obvious because as held in host of cases including *Ex parte Harris*, 748 O.G. 586; *In re Rosselete*, 146 USPQ 183; *In re Burgess*, 149 USPQ 355 and as exemplified by *In re Betz*, "the test of obviousness is not express suggestion of the claimed invention in any and all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them".

ACTION IS FINAL

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

CONCLUSION AND FUTURE CORRESPONDANCE

5. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (571) 272 0955. The examiner can normally be reached on First Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tsang Cecilia can be reached on (571) 272 0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jon Weber
Supervisory Patent Examiner

/AAM/Mohamed/AAM
July 16, 2007